Case Report

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HLA B*15:02 and carbamazepine-induced Stevens-Johnson syndrome and toxic epidermal necrolysis: first case report from Nepal with genetic analysis

Mandeep D. Joshi, MBBS[a], Bimarsh Acharya, MBBS[b,*], Surendra Sapkota, MBBS[a], Karuna Khati, MBBS[a], Dissanayake M. L. Randuwini Dissanayake, MBBS[a], Sachin Shah, MBBS[b], Jayanti Jawarchan, MD[a]

Introduction and importance: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are the severe adverse drug reactions following drugs like carbamazepine, allopurinol, and infections. Here we present A 32-year-old woman developed SJS/TEN after 7 days of carbamazepine therapy, highlighting the importance of recognizing this risk, particularly in HLA-B*1502 allele carriers.

Case presentation: A 32-year-old female developed fever, vomiting, and mucocutaneous blisters 7 days after starting carbamazepine. Lesions spread from the face to the chest, abdomen, and extremities, with throat discomfort and eye discharge. History included prior dizziness episodes.

Examination revealed denuded skin, positive Nikolsky's sign, and HLA-B*1502 allele positivity. Treatment comprised ceasing carbamazepine, fluid administration, and steroids.

Discussion: SJS/TEN manifest with distinct symptoms and often emerge within weeks of drug exposure. Carbamazepine, a frequent trigger, poses higher risks for HLA-B1502 allele carriers. Timely identification and intervention are essential to reduce mortality rates (10-40%). Treatment involves corticosteroids and supportive measures, with pre-carbamazepine HLA-B1502 screening advised, despite potential accessibility constraints.

Conclusion: This case underscores the necessity of recognizing carbamazepine-induced SJS/TEN risk, particularly in HLA-B*1502 carriers. Despite screening challenges, early intervention involving multidisciplinary specialists is essential for favorable outcomes. Increased awareness and proactive measures are vital in preventing and managing these severe reactions.

Keywords: carbamazepine, case report, Stevens-Johnson Syndrome, toxic epidermal necrolysis

Introduction

Steven-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare adverse drug reactions resulting in severe mucocutaneous disorders and detachment of the epidermis layer of the skin[1].The incidence of SJS/TEN stretches between 1 and 6 million cases per year among the population with Asians having twofold risk compared to Caucasian population[2].

Numerous drugs such as carbamazepine, allopurinol, trimethoprim-sulfamethoxazole, aminopenicillins, cephalosporins, quinolones, phenytoin, phenobarbital, and oxicam-type NSAIDs along with infections resulting from *Mycoplasma pneumoniae* and Herpes simplex virus has been found to a potential trigger for for SJS/TEN[1,2].

Here, we report a rare case of a 32-year-old female presented with mucocutaneous blisters and eye discomfort after 7 days of taking oral carbamazepine later diagnosed as SJS/TEN. This case report has been reported in line with the SCARE Criteria[3].

Case presentation:

A 32-year-old female presented with a history of fever and vomiting for 2 days. After 8 h of appearance of the first episode of fever she developed multiple, slightly raised, itchy flat painless lesions initially over face then towards the chest, abdomen, and extremities. She also complained of throat discomfort with difficulty in opening and closing eyes due to continuous yellowish-greenish discharge. Thorough history revealed that the patient had multiple episodes of dizziness in the past 8 years. Seven days prior to the presentation, she had visited the hospital for dizziness and started on 200 mg tab carbamazepine. She had been taking thyroid medication for the past 8 years and had a medical abortion 1 month back .There is no history of headache, tightness over neck, abdominal pain, insect bite, or any drug allergy in the past.

Brownish pigmentation was seen over the body including face, body and lower limbs sparing discretely over chest and

[a]Manipal College of Medical Sciences, Pokhara, Nepal and [b]KIST Medical College and Teaching Hospital, Gwarko, Lalitpur, Nepal

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*Corresponding author. Address: KIST Medical College and Teaching Hospital, Gwarko, Lalitpur, Nepal. E-mail: achaaryabimarsh456@gmail.com (B. Acharya).

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upper limbs (Figs. 1, 2, and 3). Nikolsky's signal was positive. Clinical diagnosis of TEN/SJS was made and HLA—carbamazepine & phenytoin hypersensitivity, whole blood sequencing based typing revealed HLA B*15:02 allele.

The patient's carbamazepine was stopped and a regimen of intravenous chlorpheniramine, ceftriaxone, dexamethasone, and metronidazole was given, alongside the fluid administration. Dressing was done at different parts of the body (Figs. 4 and 5)

Eye care and oral care included carboxymethylcellulose eye drop and chlorhexidine gargle. After dressing, mupirocin was applied. She was discharged after staying 2 weeks at hospital alongside the replacement of carbamazepine with sodium valproate tabs. Patient was satisfied with the treatment prohibited.

Discussion

SJS and TEN represent severe skin reactions triggered by medications. SJS typically affects less than 10% of the body surface, while TEN affects over 30%. Cases falling between these percentages are categorized as SJS/TEN overlap. These conditions are more prevalent in the elderly, women, and patients with HIV[4].

Symptoms such as fever, malaise, and sore throat are common across the disease spectrum. They usually start with erythematous macules or unusual target-like lesions on the trunk, which may progress into larger areas of redness with darkened centers. Subsequently, patients may develop flaccid blisters that separate easily from the surrounding skin when pressure is applied (positive Nikolsky sign), leading to extensive denudation of the affected skin. Oral and ocular involvement is frequent[5].

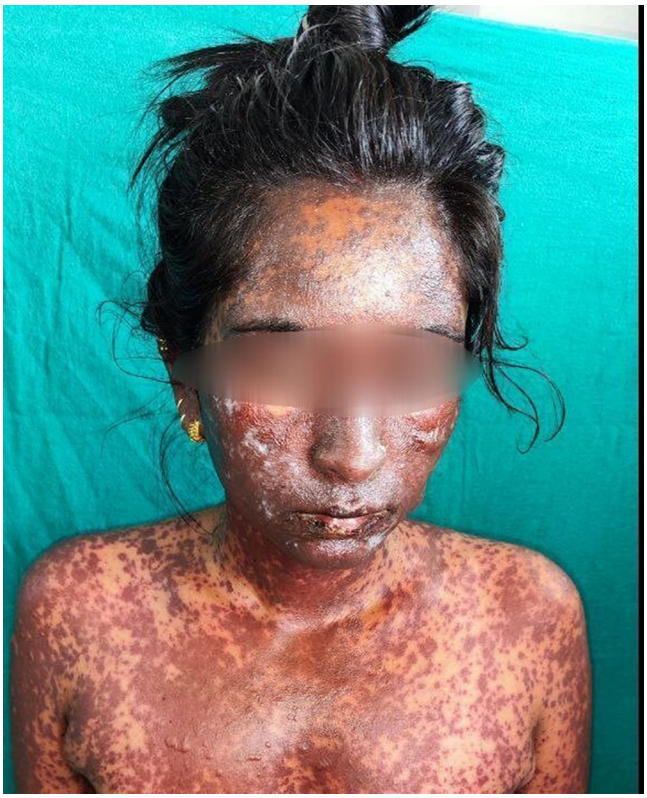

Figure 1. Lesion over upper trunk during stay in hospital.

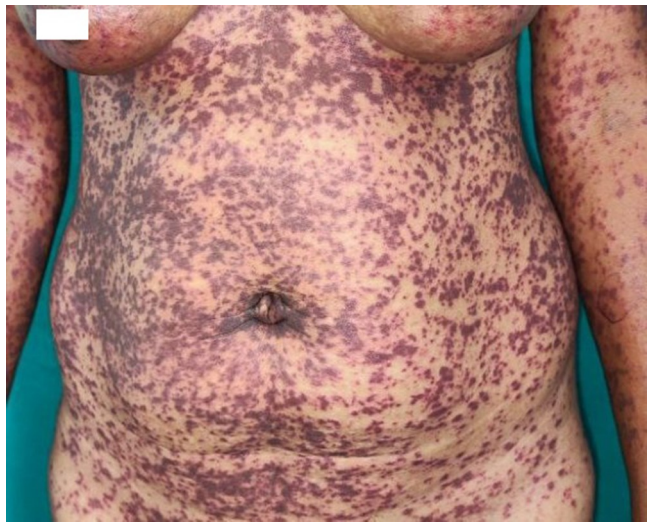

Figure 2. Lesions over lower trunk of the body.

Devi *et al* reported that carbamazepine is the most common cause of SJS/TEN, often occurring within the first 8 weeks of treatment[6]. In our case, the patient developed symptoms on the 7th day of carbamazepine therapy, progressing from SJS to TEN by the 6th day.

Drug metabolites, such as hydroxylamines and arene oxides derived from sulfonamides and aromatic anticonvulsants, respectively, bind to cell constituents if not detoxified rapidly by epoxide hydrolase. These metabolites act as haptens, rendering keratinocytes antigenic by binding to them and defect in the detoxification system may cause drug eruption[7,8].

The US Food and Drug Administration (FDA) recommends screening Asian patients for the HLA-B1502 allele before initiating carbamazepine therapy[9]. As HLA allele testing is rarely available in Nepal, the patient's blood was sent to India for testing. Our patient had the HLA-B1502 allele, supporting evidence that this combination can lead to SJS/TEN and highlighting the importance of HLA screening.

Another study reported that HLA-B4001, HLA-B4601, and HLA-B5801 were strongly protective factors against CBZ-induced SJS/TEN, whereas HLA-B1511 was a risk factor[10]. Our patient had the HLA-B*1502 allele, further supporting the evidence.

The global mortality rate of 10% to 40% emphasizes the need for early identification and prompt medical intervention based on a multidisciplinary approach. Corticosteroids are recommended by some authors, with high doses advocated[11]. Other medical therapies reported in the literature include plasmapheresis, intravenous immunoglobulins, and cyclosporine[12]. In our case, a combination of corticosteroids, antibiotics, and fluid therapy yielded a favorable response.

Early consultation with an ophthalmologist and gynecologist is crucial to prevent long-term ocular sequelae[13]. In our case, protective eye drops were added, which helped resolve the patient's presenting symptoms.

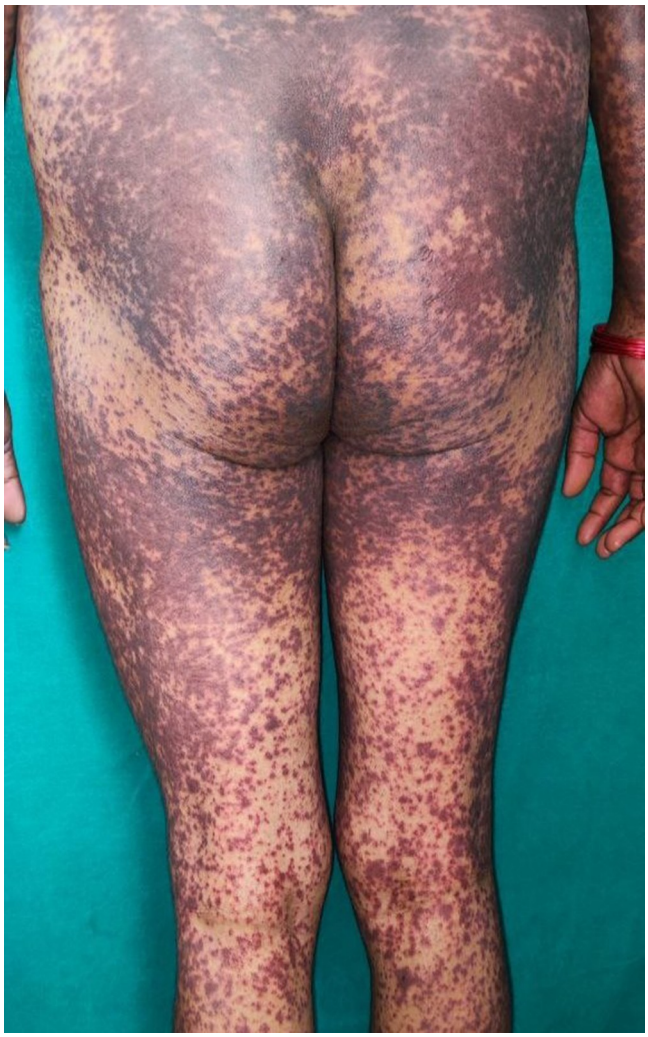

Figure 3. Erosion over bilateral gluteal regions.

Conclusion

Our case highlights the critical need to be aware of the risk associated with carbamazepine-induced SJS/TEN, especially in patients with the HLA-B*1502 allele. While screening for this allele before starting carbamazepine can be difficult in some areas, it is vital for preventing these severe reactions. Early intervention involving a team of specialists, including ophthalmologists and gynecologists, is crucial for improving outcomes in SJS/TEN cases.

Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

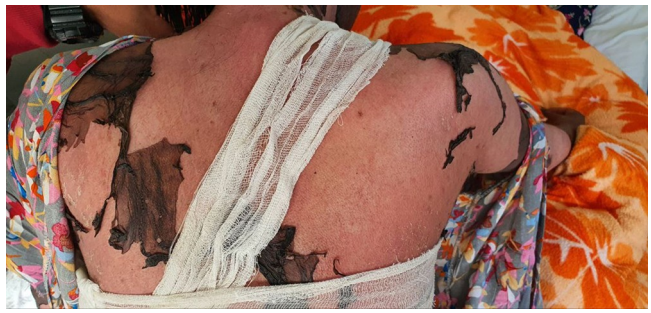

Figure 4. Dressing done over trunk for SJS and TEN at day 6 of hospital admission.

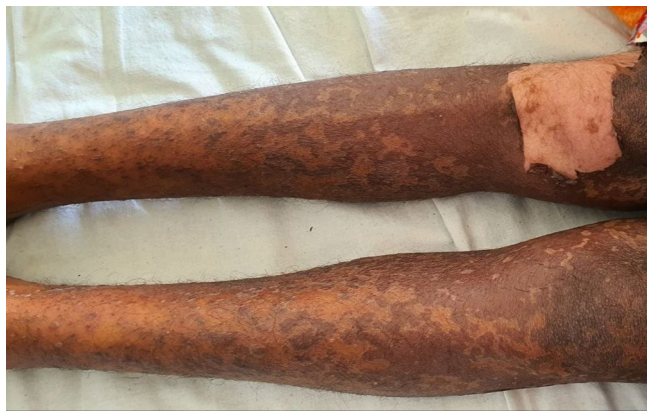

Figure 5. Dressing done over limbs for SJS and TEN at day 6 of hospital admission.

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Author contribution

All the authors individually contributed in manuscript writing, data collection and reviewing and did the final proofreading of the manuscript before submission.

Conflicts of interest disclosure

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Data availability statement

All data are available in review.

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